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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/453,234	12/01/1999	JOE BUECHLER	20015-000110	2367

7590 08/12/2002

JOE LIEBESCHUETZ
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER 8TH FLOOR
SAN FRANCISCO, CA 941113834

EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	14

DATE MAILED: 08/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/453,234	Applicant(s) BUECHLER ET AL.	
	Examiner Quang Nguyen, Ph.D	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on 5/31/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/453234 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 1-46 are pending in the present application, and they are examined on the merits herein.

Claim Objections

Claims 37, 39 and 45 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The embodiments of claims 37, 39 and 45 are already included in claims 35 (for the dependent claims 37 and 39) and 44 (for the dependent claim 45).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (WO 98/47343 with a published date of October 29, 1998) or Buechler et al. (U.S. Patent No. 6,057,098 with an effective filing date of April 04, 1997) in view of Kucherlapati et al. (WO 96/33735 with a published date of October 31, 1996, IDS, AS) and Lonberg et al. (U.S. Patent No. 5,770,429 with the effective filing date of October 10, 1995; IDS, AD).

Claims 1-16 and 46 are drawn to a method of producing a human antibody display library comprising providing a transgenic mouse whose genome comprises a plurality of human immunoglobulin genes that can be expressed to produce a plurality of human antibodies; isolating a population of nucleic acids encoding human antibody chains from lymphatic cells of the transgenic mouse; forming a library of display packages displaying the antibody chains, wherein a library member comprises a nucleic acid encoding an antibody chain, and the antibody chain is displayed from the package, wherein the library comprises at least 100 members at least 50% of which comprise

nucleic acids encoding human antibody chains showing at least 10^9 M^{-1} affinity for the same target and no library member constitutes more than 50% of the library.

Claims 17-34 are directed to a method of producing a human Fab phage display library, comprising: providing a transgenic mouse whose genome comprises a plurality of human immunoglobulin genes that can be expressed to produce a plurality of human antibodies; isolating populations of nucleic acids respectively encoding human antibody heavy chains and human antibody light chains from lymphatic cells of the transgenic mouse; cloning the populations into multiple copies of a phage display vector to produce a display library, wherein a library member comprises a phage capable of displaying from its outersurface a fusion protein comprising a phage coat protein, a human antibody light chain or human antibody heavy chain, wherein in at least some members, the human antibody heavy or light chain is complexed with a partner human antibody heavy or light chain, the complex forming a Fab fragment to be screened, wherein the library comprises at least 100 members at least 50% of which comprise nucleic acids encoding Fab fragments showing at least 10^9 M^{-1} affinity for the same target and no library member constitutes more than 50% of the library.

Claims 35-45 are directed to a library comprising nucleic acid segments encoding human antibody chains with limitations recited in the claims.

Gray et al. teach a method for preparing a library of replicable genetic packages displaying from their outersurface polypeptides including antibodies, particularly Fab fragments (page 3, lines 20-27). A library member comprises a phage displaying from its outer surface a fusion protein comprising a phage coat protein, an antibody light

chain or heavy chain variable domain and a tag. In at least some members, the antibody heavy or light chain is complexed with a partner antibody heavy or light chain variable domain chain, the complex forming a Fab fragment to be screened. The fusion protein and/or the partner antibody heavy or light chain are encoded by segment(s) of the genome of the phage. A tag is also fused to either the fusion protein or the partner antibody heavy or light chain, and the tag is the same in different library members. The number of copies of the fusion protein and the partner antibody chain displayed per phage vary between library members (page 4, lines 8-21). The antibody encoding sequences can be obtained from lymphatic cells of a human or nonhuman animal, usually the cells have been immunized, in which case immunization is performed *in vivo* before harvesting the cells or *in vitro* after harvesting the cells, or both, and often spleen cells of an immunized animal are a preferred source of material (page 18, lines 22-27). Gray et al further teach that the library or a fraction of thereof is contacted with a receptor having a specific affinity for the tag under conditions whereby library members displaying at least two copies of the fusion protein are preferentially bound to immobilized receptor by multivalent bonds between the receptor and the at least two copies of the tag. Library members bound to the receptor are then separated from unbound library members to produce a sub-library enriched relative to the library for members displaying at least two copies of the fusion protein (page 4, lines 21-30). Additionally, a polyvalent phage display library can be further screened by contacting the library with a target lacking specific affinity for the tag moiety and separating library members bound to the target via their displayed polypeptides from unbound library

members. DNA segments encoding polypeptides having specific affinity for a target can be subcloned in an expression vector, and the polypeptides expressed in host cells (page 5, lines 17-24). Gray et al. further teach that the disclosed library comprises at least four different nucleic acid segments, at least 90% of segments in the library encode polypeptides showing specific affinity for a target and no library member constitutes more than 50% of the library. In some libraries, at least 95% of library members encode polypeptides having specific affinity for a target and such libraries have at least 4, 10, 20, 50, 100, 1000, 10,000 or 100,000 different coding sequences, and no member constitutes more than 50%, 25% or 10% of the total coding sequences in the library (page 5, lines 29-37 and page 28, lines 24-28). As defined by Gray et al., specific binding between an antibody and an antigen means a binding affinity of at least 10^6 M^{-1}, and more preferably 10^7 M^{-1}, 10^8 M^{-1}, 10^9 M^{-1} or 10^{10} M^{-1} (page 8, second last paragraph). Buechler et al. disclose the same teachings as those of Gray et al.

However, neither Gray et al. nor Buechler et al. disclose a method of producing a human antibody display library or a human Fab phage display library using isolated populations of nucleic acids from lymphatic cells of a transgenic mouse whose genome comprises a plurality of human immunoglobulin genes that can be expressed to produce a plurality of human antibodies. Nor do the references teach the same method wherein the nucleic acids encode variable regions of the antibody chains and the display vector comprises a segment encoding a human constant region and the cloning joins a nucleic acid encoding a variable region in-frame with the segment encoding the human constant region, or wherein the plurality of human genes is free of human lambda light

chain genes or wherein there are no more than 40 human VH or VL genes included in the plurality of human genes.

Kucherlapati et al. teach that the genes encoding the repertoire of immunoglobulins produced by the immunized animal can be used to generate a library of immunoglobulins to permit screening for those variable regions which provide the desired affinity using the phage display techniques (page 11, lines 15-37). Clones from the library which have the desired characteristics can then be used as a source of nucleotide sequences encoding the desired variable regions for further manipulation to generate antibodies or analogs with these characteristics using standard recombinant techniques (page 3, lines 6-15). One such immunized animal is a transgenic XenoMouse, being immunized with a desired antigen, and wherein said transgenic mouse is substantially incapable of producing endogenous heavy or light immunoglobulin chain, but capable of producing immunoglobulins with both human variable and constant regions (page 2, lines 10-15 and lines 22-31). In the Xenomouse, the human heavy chain YAC, yH1C comprising of 870 kb of the human variable region, the entire D and J_H region, human μ, δ, and $\gamma 2$ constant regions and the mouse 3' enchancer; and human light chain YAC, yK2 comprising of 650 kb of the human kappa chain proximal variable region (V_κ), the entire J_κ region, and C_κ with its flanking sequences that contain the kappa deleting element are used (page 6, lines 1-8). Moreover, Kucherlapati et al. disclose that the genes encoding antibodies can be prepared from primary B cells of the blood or lymphoid tissue (spleen, tonsils, lymph nodes, bone marrow) of the immunized animal (page 3, lines 1-3). Kucherlapati et al.

further teach that the combination of phage display technology with the XenoMouse offers a significant advantage over previous applications of phage display in obtaining high affinity antibodies to human proteins via somatic mutation by repeated immunizing the XenoMouse with human proteins (page 13, lines 1-7).

Apart from the Xenomouse, Lonberg et al. disclose another transgenic mouse comprising an inactivated endogenouse mouse immunoglobulin gene locus, and said transgenic mouse further containing in its genome transgenes comprising a 670 to 830 kb human genomic heavy chain fragment containing members of all six of the known V_H families, the D and J gene segments, as well as the μ, δ, $\gamma 3$, $\gamma 1$ and $\alpha 1$ constant regions (column 30, lines 9-20); and a human genomic light chain 450 kb fragment or in combination with another genomic 400 kb fragment containing all of C_κ, the 3' enhancer, all J segments and at least five to at least 20 different V segments (column 53, lines 40-67). Lonberg et al. also noted that human heavy chain locus is estimated to consist of approximately 200 V gene segments (current data supports the existence of about 50-100 V gene segments) spanning 2 Mb (column 29, lines 65-67). Lonberg et al. further teach that a hybridoma composed of a B cell obtained from the disclosed transgenic mouse produces an immunoglobulin having a binding constant of at least 10^{10} M^{-1} for binding to a predetermined human antigen (See the claims).

Accordingly, at the time of the instant invention it would have been obvious to the ordinary skilled artisan to modify the method for preparing a library of replicable genetic packages displaying from their outersurface polypeptides including antibodies, particularly Fab fragments taught by Gray et al. by using antibody encoding sequences

obtained from lymphatic cells of the XenoMouse as taught by Kucherlapati et al. or from lymphatic cells of the transgenic mouse disclosed by Lonberg et al. to arrive at the instant claimed invention. One of ordinary skilled artisan would have been motivated to carry out the modification because as mentioned above, Kucherlapati teach that the combination of phage display technology with a transgenic mouse such as the XenoMouse (not necessarily limited to a XenoMouse) offers a significant advantage over previous applications of phage display for obtaining high affinity antibodies (e.g. those with 10^9 M^{-1} or 10^{10} M^{-1} affinity) to any human protein via somatic mutation by repeated immunizing the XenoMouse with human proteins (page 13, lines 1-7). It would be unethical and impossible to administer repeatedly into a human any and all desired antigen or normal human proteins to generate high affinity antibodies against the desired antigen or normal human proteins. One of ordinary skilled in the art would have a predicted expectation of success for the modified method in view of the combined teachings of Gray et al., Kucherlapati et al. and Lonberg et al. With regard to recited method steps wherein the nucleic acids encode variable regions of the antibody chains and the display vector comprises a segment encoding a human constant region and the cloning joins a nucleic acid encoding a variable region in-frame with the segment encoding the human constant region, these are standard molecular biology techniques and would have been within the scope of skills of the ordinary artisan at the time of the instant invention. With respect to claim 46 specifically reciting the limitation of amplifying the population of nucleic acids using a set of primers selected based on which human immunoglobulin genes from the full complement of human

immunoglobulin genes are present in the genome of the transgenic mouse, it would also have been obvious and within the scope of skill for an ordinary skilled artisan at the effective filing date of the present application to design a set of primers selected based on which human immunoglobulin genes present in the genome of the transgenic mouse of Lonberg et al. or of XenoMouse or of other transgenic mouse whose genome comprising less than the full complement of human immunoglobulin genes present in a human being. The art and the level of skill for designing customized primers for amplifying human immunoglobulin genes present in a transgenic mouse are high and routine as evidenced by the teachings of Gray et al. who showed that a library of replicable genetic packages containing members encoding antibodies having specific affinity for a target having at least 100, 1000, 10,000 or 100,000 different coding sequences and no member constitutes more than 50%, 25% or 10% of the total sequences in the library (see page 5, lines 29-37 and page 28, lines 24-28), wherein the specific binding between an antibody and an antigen of at least 10^6 M^{-1}, and more preferably 10^7 M^{-1}, 10^8 M^{-1}, 10^9 M^{-1} or 10^{10} M^{-1} (see page 8, second last paragraph), can be obtained without relying on the set of customized primers disclosed in the presently claimed invention (see also Figures 1 and 2).

The claimed library of the instant invention would also become obvious to one of ordinary skilled artisan because the method for making a library having the recited limitations is obvious for the reasons cited above.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 10/05/2001 in Paper No. 8 (pages 7-11) have been fully considered.

Applicants mainly argue that the cited Kucherlapati reference does not provide a reasonable expectation of success for the making of a library of the presently claimed invention for two main reasons. First, the XenoMouse expressing human immunoglobulin genes typically contain significantly fewer such genes than are present in a natural human, therefore one might expect the use of less than the full repertoire of genes might limit capacity of such an animal to generate high affinity antibodies compared with a natural human. As such, the combination of phage display with the Xenomouse would not achieve even antibodies of 10^8 M^{-1} affinity. Second, the phage display technique involves a random assortment of heavy and light chains in the cloning step into the phage vector. In the course of random assortment, naturally selected pairings of heavy and light chain are separated and usually not reconstructed because in practice one can not screen all the possible permutations of heavy and light chains that may be created by random recombination. Therefore, the loss of naturally selected pairs giving rise to antibodies having highest affinities would reduce the frequency of high affinity antibodies. Applicants further argue that Kucherlapati provides no indication of how many antibodies he had to screen to obtain the few high affinity antibodies shown in Table 4 of Kucherlapati, and therefore it is not apparent that Kucherlapati was able to isolate high affinity human antibodies at high frequency directly

from the Xenomouse in contrast to the instantly claimed invention. Examiner respectfully finds Applicants' arguments to be unpersuasive for the following reasons.

First, in response to applicant's arguments against the Kucherlapati reference, one cannot show nonobviousness by attacking the reference individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Gray et al. or Buechler et al. essentially disclose the same phage display techniques utilized in the presently claimed invention, Lonberg et al. teach the transgenic mouse (other than the XenoMouse of Kucherlapati) whose genome comprises a plurality of human immunoglobulin genes that is also contemplated by Applicants for the practice of the presently claimed invention (see specification, page 94, lines 21-24), and that Kucherlapati clearly teaches the concept of combining phage display technology with an immunized transgenic mouse whose genome comprises a plurality of human immunoglobulin genes such as the XenoMouse for obtaining high affinity human antibodies via somatic mutation by repeated immunization with human proteins. Additionally, Gray et al. who showed that a library of replicable genetic packages containing members encoding antibodies having specific affinity for a target having at least 100, 1000, 10,000 or 100,000 different coding sequences and no member constitutes more than 50%, 25% or 10% of the total sequences in the library (see page 5, lines 29-37 and page 28, lines 24-28), wherein the specific binding between an antibody and an antigen of at least 10^6 M^{-1}, and more preferably 10^7 M^{-1}, 10^8 M^{-1}, 10^9 M^{-1} or 10^{10} M^{-1} (see page 8, second last paragraph), can be obtained

without relying on the set of customized primers disclosed in the presently claimed invention.

Second, in contrary to Applicants' assertion that one might expect the use of less than the full repertoire of genes in a transgenic mouse might limit capacity of such an animal to generate high affinity antibodies compared with a natural human, high affinity human antibodies to human IL-8 could be isolated from Xenomouse (affinity in the range 10^9 to 10^{11} M^{-1}, see Table 4 of the Kucherlapati reference) as well as high affinity human antibodies to human CD4 could be isolated from a transgenic mouse of Lonberg et al. that does not comprise a full complement of human immunoglobin genes present in a human being (a binding constant of at least 10^{10} M^{-1}, see the claims of U.S. Patent No. 5,770,429). Moreover, Kucherlapati et al. teach that the combination of phage display technology with the XenoMouse offers a significant advantage over previous applications of phage display in obtaining high affinity antibodies to human proteins via somatic mutation by repeated immunizing the XenoMouse with human proteins (page 13, lines 1-7). One of ordinary skilled artisan would also be motivated to repeated immunizing the transgenic mouse of Lonberg et al. with human proteins to generate high affinity human antibodies to human proteins.

Third, with respect to Applicants' argument that the loss of naturally selected pairs giving rise to antibodies having highest affinities due to the nature of phage display technique would reduce the frequency of high affinity antibodies, even without the advantage offered by somatic mutation by repeated immunizing a transgenic mouse with human protein, Burton et al. (Proc. Natl. Acad. Sci. USA 88:10134-10137, 1991)

still isolated a large array of human monoclonal antibodies to type 1 human immunodeficiency virus with affinity constants of or greater than 10^8 M^{-1} (including 10^9 M^{-1}, see Fig. 2) using the phage display technique. Furthermore, Gray et al. or Buechler et al. essentially discloses the same phage display technique utilized in the instantly claimed invention, and the transgenic mouse of Lonberg et al. is also contemplated by Applicants for the practice of the presently claimed invention (page 94, lines 21-24). As such, it is reasonable to expect one of ordinary skilled in the art to have a predicted expectation of success for making of a library of the presently claimed invention using the modified method resulting from the combined teachings of Gray et al. or Buechler et al., Kucherlapati et al. and Lonberg et al.

With respect to the newly added claim 46, Applicants argue "The Kucherlapati reference does not disclose or suggest use of a customized set of primers as specified in claim 46. Kucherlapati's only teaching regarding primers is to use Marks' set of primers. Further, in his brief and prophetic discussion regarding use of phage display on a Xenomouse, Kucherlapati does not provide any indication that modifications to previous phage display protocols might be desirable to adapt phage display to use in combination with a transgenic mouse....[t]he use of customized primers can result in a different population of antibodies than that would result from using Mark's primers as recommended by Kucherlapti". Examiner respectfully finds Applicants' argument to be unpersuasive for the same reasons discussed in the preceding paragraphs. The deficiencies of the Kucherlapati reference can be cured by the teachings of Gray et al. or Buechler et al. and Lonberg et al. It is noted that Applicants failed to provide any

objective evidence for why one of ordinarily skilled artisan would limit exclusively the teachings of Kucherlapati et al. with the use of Marks' set of primers, and that the rejection is based on combinations of the aforementioned references. It would also have been obvious and within the scope of skill for an ordinary skilled artisan at the effective filing date of the present application to design a set of primers selected based on which human immunoglobulin genes from the full complement of human immunoglobulin genes that are present in the genome of the transgenic mouse such as the transgenic mouse of Lonberg et al., without exclusively dependent on Mark's set of primers. There is nowhere in the Kucherlapati reference containing any negative teachings regarding to customized primers other than Mark's set of primers should not be used. Examiner would also like to note that one of skilled in the art has the ability to think, and the art and the level of skill for designing customized primers for amplifying human immunoglobulin genes present in a transgenic mouse are high and routine. Moreover, Gray et al. already showed that a library of replicable genetic packages containing members encoding antibodies having specific affinity for a target having at least 100, 1000, 10,000 or 100,000 different coding sequences and no member constitutes more than 50%, 25% or 10% of the total sequences in the library (see page 5, lines 29-37 and page 28, lines 24-28), wherein the specific binding between an antibody and an antigen of at least $10^6\ M^{-1}$, and more preferably $10^7\ M^{-1}$, $10^8\ M^{-1}$, $10^9\ M^{-1}$ or $10^{10}\ M^{-1}$ (see page 8, second last paragraph), can be obtained without relying on the set of customized primers disclosed in the presently claimed invention (see also Figures

1 and 2). Furthermore, Examiner notes that the claims do not recite any characteristics of a set of customized primers that yield unexpected results as asserted by Applicants.

Accordingly, claims 1-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. or Buechler et al. in view of Kucherlapati et al. and Lonberg et al., for the reasons set forth above.

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Crouch Deborah, at (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER